

AMENDMENTS TO THE CLAIMS

This listing of the claims replaces all prior listings and versions:

1. (original): A method of selecting a switching system, the switching system comprising: (i) a first component comprising a first molecule and (ii) a second component comprising a second molecule, in which the first molecule binds to the second molecule in a manner modulatable by a ligand, and (iii) a third component comprising the ligand, the method comprising the steps of.

- (a) contacting one or more candidate first molecules with one or more candidate second molecules in the presence of one or more ligands,
 - (b) selecting a complex of the three components;
 - (c) optionally isolating and/or identifying the unknown components of the complex;
 - (d) comparing the binding of the first molecule component of the complex to the second molecule component of the complex in the presence and absence of the ligand component of the complex; and
 - (e) selecting complexes where said binding differs in the presence and absence of the ligand component,
- in which at least one component is provided in the form of a library of members.

2. (original): A method according to Claim 1, in which at least one of the candidate first molecules comprises a non-naturally occurring binding domain which binds to the second molecule.

3. (previously presented): A method according to claim 1, in which one of the first molecule and second molecule comprises a nucleic acid binding molecule, and the other of the first and second molecules comprises a nucleic acid.

4. (previously presented): A method according to Claim 1, in which one or both of the candidate nucleic acid and nucleic acid binding molecules is provided as a plurality of molecules.

5. (original): A method according to Claim 4, in which the nucleic acid binding molecule is provided as a library of nucleic acid binding molecules.

6. (previously presented): A method according to Claim 4, in which a single target nucleic acid is used.

7. (previously presented): A method according to Claim 4, in which one of the components isolated and/or identified in step (c) is a ligand component.

8. (previously presented): A method according to claim 4, in which one of the components isolated in step (c) is a nucleic acid binding molecule component.

9. (previously presented): A method according to claim 4, in which the nucleic acid is provided as a library of nucleic acid sequences, the sequences being related to one another by sequence homology.

10. (previously presented): A method according to claim 4, in which a plurality of candidate ligands are used.

11. (previously presented): A method according to claim 4, in which the ligands are provided as a library of ligands.

12. (previously presented): A method according to claim 4, in which the candidate nucleic acid binding molecules are polypeptides.

13. (previously presented): A method according to claim 4, in which the polypeptides are at least partly derived from DNA binding proteins, preferably transcription factors.

14. (previously presented): A method according to claim 4, in which the candidate nucleic acid binding molecules are derived from zinc finger transcription factors.

15. (previously presented): A method according to claim 4, in which the candidate nucleic acid binding molecules are provided as a phage display library.

16. (previously presented): A method according to claim 4, in which the ligand is selected from Distamycin A, Actinomycin D and echinomycin.

17. (previously presented): A switching system comprising a gene switch, in which the switching system has been selected by a method according to claim 4.

18. (previously presented): A method of regulating transcription from a nucleic acid sequence comprising providing a target nucleic acid to which a nucleic acid binding molecule selected according to the method of claim 4 binds in a manner modulatable by a ligand and binding the nucleic acid binding molecule to the target nucleic acid such that transcription is regulated.

19 and 20. (canceled).

21. (previously presented): A method of modulating the expression of one or more genes, said method comprising administering a nucleic acid binding molecule and a ligand selected according to the method of claim 4 to a cell, in which the regulatory sequences of the genes comprise a target nucleic acid selected according to the method of claim 4.

22. (original): A method of modulating the expression of one or more nucleotide sequences of interest in a host cell which host cell comprises a nucleic acid sequence capable of directing the expression of a nucleic acid binding molecule and a target nucleic acid sequence to which the nucleic acid binding molecule binds in a manner modulatable by a ligand, which method comprises administering said ligand to the cell and wherein the nucleic acid binding molecule is heterologous to the host cell.

23. (previously presented): A method according to Claim 21 wherein the host cell is a plant cell.

24. (original): A method according to Claim 23, in which the plant cell is part of a plant and the target sequence is part of a regulatory sequence to which the nucleotide sequence of interest is operably linked, said regulatory sequence being preferentially active in the male or female organs of the plant.

25. (original): A non human transgenic organism comprising a target nucleic acid sequence and a nucleic acid sequence capable of directing the expression of a nucleic acid binding molecule which binds to the target nucleic acid in a manner modulatable by a ligand, in which the target nucleic acid sequence and/or nucleic acid sequence are heterologous to the organism.

26. (original): A transgenic non-human organism according to Claim 25 which is a plant.

27. (previously presented): A method according to Claim 1, in which each of the first and second molecules comprises a polypeptide.

28. (original): A method according to Claim 27, in which the first molecule comprises a polypeptide binding protein and the second molecule comprises a polypeptide.

29. (previously presented): A method according to Claim 27, in which one or both of the first and second molecules is provided as a library of polypeptides.

30. (previously presented): A method according to Claim 27, in which the ligands are provided as a library of ligands.

31. (previously presented): A method according to claim 27, in which the ligand is an immunoglobulin molecule, preferably an antibody molecule.

32. (previously presented): A method according to claim 27, in which the first molecule is a nucleic acid binding protein capable of binding to nucleic acid.

33. (original): A method according to Claim 32, in which the nucleic acid binding protein binds to nucleic acid in a manner modulatable by the second molecule.

34. (currently amended): A switching system comprising a protein switch comprising: (i) a first component comprising a first polypeptide and (ii) a second

component comprising a second polypeptide, in which the first polypeptide binds to the second polypeptide in a manner modulatable by a ligand, and (iii) a third component comprising the ligand and in which the switching system has been selected by the method of claim 27 a method comprising the steps of:

- (a) contacting one or more candidate first polypeptides with one or more candidate second polypeptides in the presence of one or more ligands,
 - (b) selecting a complex of the three components;
 - (c) optionally isolating and/or identifying the unknown components of the complex;
 - (d) comparing the binding of the first polypeptide component of the complex to the second polypeptide component of the complex in the presence and absence of the ligand component of the complex; and
 - (e) selecting complexes where said binding differs in the presence and absence of the ligand component,
- in which at least one component is provided in the form of a library of members.

35. (previously presented): A method of regulating transcription from a nucleic acid sequence comprising providing a target nucleic acid to which a nucleic acid binding protein selected by the method according to claim 33 binds and binding the nucleic acid binding protein to the target nucleic acid, thereby regulating transcription.

36 and 37. (canceled).

38. (original): A method of modulating the expression of one or more genes, said method comprising administering a nucleic acid binding protein and a ligand selected according to a method according to Claim 33 to a cell, in which the regulatory sequences of the genes comprise a target nucleic acid to which the nucleic acid binding protein binds in a manner modulatable by a ligand.

39. (original): A method of modulating the expression of one or more nucleotide sequences of interest in a host cell which host cell comprises a first nucleic acid sequence capable of directing the expression of a nucleic acid binding protein, a second nucleic acid sequence capable of directing the expression of a second polypeptide, the binding between the nucleic acid binding to the second polypeptide being modulatable by a

ligand, and a target nucleic acid sequence to which the nucleic acid binding protein binds in a manner modulatable by a second polypeptide, which method comprises administering said ligand to the cell.

40. (original): A method according to Claim 39, in which the nucleic acid binding protein is heterologous to the host cell.

41. (previously presented): A method according to Claim 39 wherein the host cell is a plant cell.

42. (previously presented): A method according to Claim 41, in which the plant cell is part of a plant and the target sequence is part of a regulatory sequence to which the nucleotide sequence of interest is operably linked, said regulatory sequence being preferentially active in the male or female organs of the plant.

43. (original): A non human transgenic organism comprising a target nucleic acid sequence, a first nucleic acid sequence capable of directing the expression of a nucleic acid binding protein, and a second nucleic acid sequence capable of directing the expression of a second polypeptide which binds to the nucleic acid binding protein in a manner modulatable by a ligand, in which the nucleic acid binding protein binds to the target nucleic acid sequence in a manner modulatable by binding of the second polypeptide.

44. (previously presented): An organism according to Claim 43, in which any or all of the first nucleic acid sequence, the second nucleic acid sequence, and the target nucleic acid sequence are heterologous to the organism.

45. (previously presented): A transgenic nonhuman organism according to Claim 43 which is a plant.

46. (previously presented): A method according to claim 1, in which the first molecule component of the complex has a higher affinity for the second molecule component of the complex in the presence of the ligand component than in the absence of the ligand component.

47. (previously presented): A method according to claim 1, in which the first molecule component of the complex has a higher affinity for the second molecule component of the complex in the absence of the ligand component than in the presence of the ligand component.